AMENDMENTS TO THE CLAIMS

1. (Original) An agent for inhibiting an excessive effect of NAD(P)H oxidase, which comprises a compound that does not substantially inhibit the effect of leukocyte NADPH oxidase but inhibits the effect of NAD(P)H oxidase in a tissue other than leukocyte.

2. (Original) The agent of claim 1, wherein the tissue other than leukocyte is a tissue of a vascular cell, the heart, the kidney, the retina, the microglia or a tumor cell.

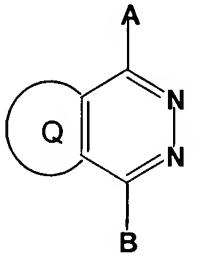
3. (Currently Amended) The agent of claim 1 ~~or 2~~, wherein the excessive effect of NAD(P)H oxidase is caused by diabetes, hypertension, hyperlipidemia, obesity, smoking, heart failure, cardiac hypertrophy, ischemic heart diseases, angioplasty or ischemia-reperfusion in organ transplantation.

4. (Currently Amended) The agent of claim 1 ~~or 2~~, wherein the excessive effect of NAD(P)H oxidase is caused by cancer or dementia.

5. (Currently Amended) The agent of claim 1 ~~or 2~~, wherein the excessive effect of NAD(P)H oxidase is caused by intake of chemicals.

6. (Original) The agent of any one of claims 1 to 5, wherein the compound that does not substantially affect leukocyte NADPH oxidase but inhibits an excessive effect of NAD(P)H oxidase in a tissue other than leukocyte is a bicyclic pyridazine compound represented by the following formulas (I) to (VIII) or a pharmacologically acceptable salt thereof:

formula (I)

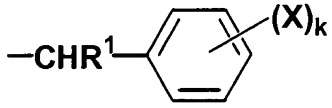


(I)

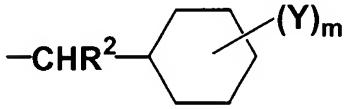
wherein A is C_3-C_6 alkyl, C_5-C_7 cycloalkyl, or phenyl, thienyl, furyl, thiazolyl, phenoxy, C_7-C_9 phenylalkyl, phenylthio, nitrogen-containing saturated ring group, pyridyl or imidazolyl, each optionally having one or more substituents selected from C_1-C_4 alkyl, C_1-C_4 alkoxy and halogen,

B is -NH-D

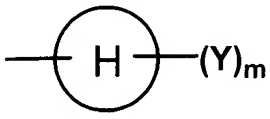
[D is



wherein R^1 is hydrogen or C_1-C_4 alkyl, X is halogen, C_1-C_4 alkyl or C_1-C_4 alkoxy, and k is an integer of 0 to 3, when k is an integer of 2 or more, multiple Xs may be the same or different,



wherein R^2 is hydrogen or C_1-C_4 alkyl, Y is C_1-C_4 alkyl or C_1-C_4 alkoxy, and m is an integer of 0 to 6, when m is 2 or more, multiple Ys may be the same or different, and any two Ys may be joined to form optionally branched C_1-C_6 alkylene,



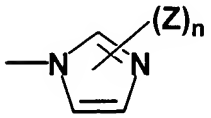
wherein ring H is C_5-C_7 cycloalkyl, and Y and m are as defined above,

-CHR^3R^4

wherein R^3 is C_1-C_5 alkyl, and R^4 is C_5-C_8 cycloalkyl or thienyl,

or C_3-C_8 alkyl]

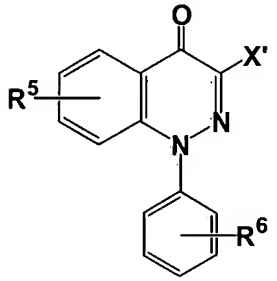
or



wherein Z is C_1 -C_4 alkyl or phenyl, and n is an integer of 0 to 2, when n is 2, these Zs may be the same or different, and

Q is a benzene ring, a furan ring or a thiophene ring optionally substituted by C_1 -C_4 alkyl,

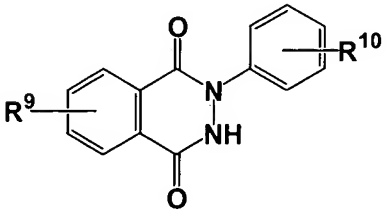
formula (II)



(II)

wherein R^5 and R^6 are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, and X' is -$COOR^7$ (R^7 is hydrogen or optionally substituted C_1-C_6 alkyl), -$CONH_2$, -CN, -COR^8 (R^8 is optionally substituted C_1-C_6 alkyl or optionally substituted aryl), -NH_2, -NO_2 or -OR^7 (R^7 is as defined above),

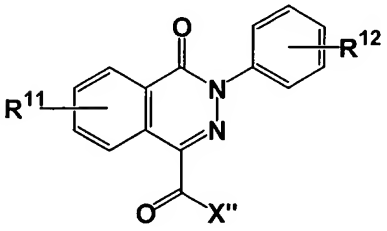
formula (III)



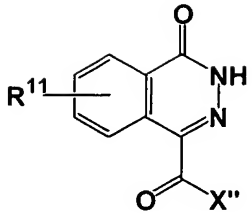
(III)

wherein R^9 and R^{10} are each independently hydrogen, C_1 -C_6 alkyl, C_1 -C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl,

formulas (IV) and (V)



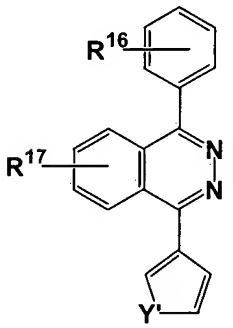
(IV)



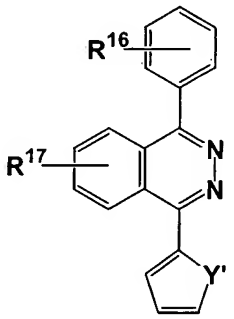
(V)

wherein R^{11} and R^{12} are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, and X" is $-OR^{13}$ (R^{13} is hydrogen, C_1-C_6 alkyl or aryl) or $-NR^{14}R^{15}$ (R^{14} and R^{15} are each independently hydrogen, C_1-C_6 alkyl or aryl,

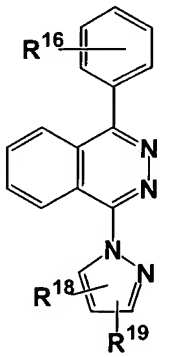
formulas (VI), (VII) and (VIII)



(VI)



(VII)



(VIII)

wherein R^{16} and R^{17} are each independently hydrogen, C_1 -C_6 alkyl, alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, R^{18} and R^{19} are each independently hydrogen or C_1 -C_6 alkyl, and Y' is oxygen or sulfur.

7. (Currently Amended) A pharmaceutical composition for the diseases caused by an excessive effect of NAD(P)H oxidase, which comprises the agent of ~~any one of claims 1 to 6~~claim 1 as an active ingredient.

8. (Original) The pharmaceutical composition of claim 7, which is administered simultaneously with a hypolipidemic agent, an antihypertensive agent, a hypoglycemic agent, a vasodilator, an antiplatelet agent, an anticoagulant, a brain

protective agent, an anticancer agent, a diuretic agent, a cardiotonic agent, an analgesic agent, an antiedemic agent, a thrombolytic agent, an immunosuppressant, a steroid, a vitamin or an antioxidant, or administered separately therefrom, or administered sequentially therewith.

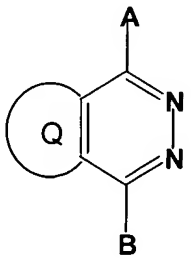
9. (New) The agent of claim 2, wherein the excessive effect of NAD(P)H oxidase is caused by diabetes, hypertension, hyperlipidemia, obesity, smoking, heart failure, cardiac hypertrophy, ischemic heart diseases, angioplasty or ischemia-reperfusion in organ transplantation.

10. (New) The agent of claim 2, wherein the excessive effect of NAD(P)H oxidase is caused by cancer or dementia.

11. (New) The agent of claim 2, wherein the excessive effect of NAD(P)H oxidase is caused by intake of chemicals.

12. (New) The agent of any one of claims 9 to 11, wherein the compound that does not substantially affect leukocyte NADPH oxidase but inhibits an excessive effect of NAD(P)H oxidase in a tissue other than leukocyte is a bicyclic pyridazine compound represented by the following formulas (I) to (VIII) or a pharmacologically acceptable salt thereof:

formula (I)



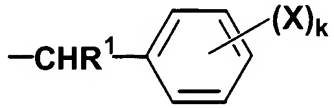
(I)

wherein A is C_3-C_6 alkyl, C_5-C_7 cycloalkyl, or phenyl, thienyl, furyl, thiazolyl, phenoxy, C_7-C_9 phenylalkyl, phenylthio, nitrogen-containing saturated ring group, pyridyl or

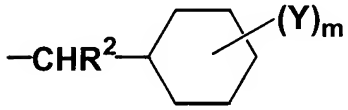
imidazolyl, each optionally having one or more substituents selected from C_1-C_4 alkyl, C_1-C_4 alkoxy and halogen,

B is -NH-D

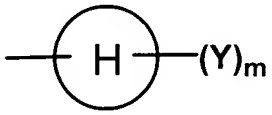
[D is



wherein R^1 is hydrogen or C_1-C_4 alkyl, X is halogen, C_1-C_4 alkyl or C_1-C_4 alkoxy, and k is an integer of 0 to 3, when k is an integer of 2 or more, multiple Xs may be the same or different,



wherein R^2 is hydrogen or C_1-C_4 alkyl, Y is C_1-C_4 alkyl or C_1-C_4 alkoxy, and m is an integer of 0 to 6, when m is 2 or more, multiple Ys may be the same or different, and any two Ys may be joined to form optionally branched C_1-C_6 alkylene,



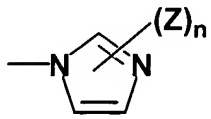
wherein ring H is C_5-C_7 cycloalkyl, and Y and m are as defined above,

$-CHR^3R^4$

wherein R^3 is C_1-C_5 alkyl, and R^4 is C_5-C_8 cycloalkyl or thienyl,

or C_3-C_8 alkyl]

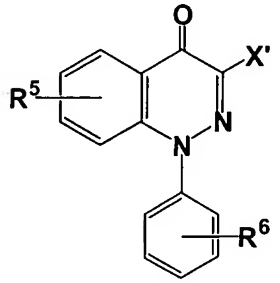
or



wherein Z is C_1-C_4 alkyl or phenyl, and n is an integer of 0 to 2, when n is 2, these Zs may be the same or different, and

Q is a benzene ring, a furan ring or a thiophene ring optionally substituted by C_1-C_4 alkyl,

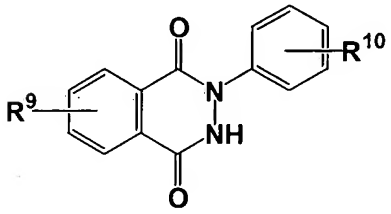
formula (II)



(II)

wherein R^5 and R^6 are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, and X' is $-COOR^7$ (R^7 is hydrogen or optionally substituted C_1-C_6 alkyl), $-CONH_2$, -CN, $-COR^8$ (R^8 is optionally substituted C_1-C_6 alkyl or optionally substituted aryl), $-NH_2$, $-NO_2$ or $-OR^7$ (R^7 is as defined above),

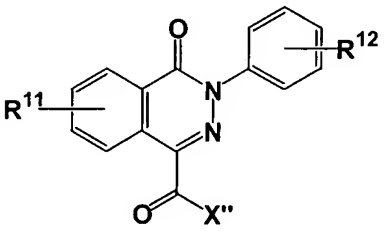
formula (III)



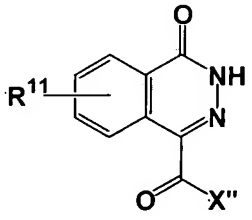
(III)

wherein R^9 and R^{10} are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl,

formulas (IV) and (V)



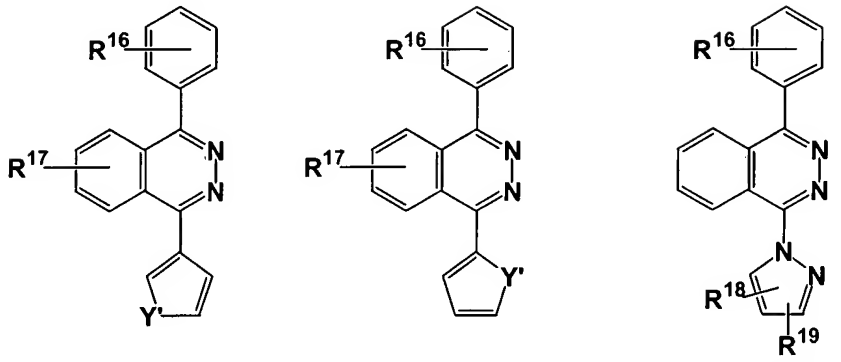
(IV)



(V)

wherein R^{11} and R^{12} are each independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, and X'' is $-OR^{13}$ (R^{13} is hydrogen, C_1-C_6 alkyl or aryl) or $-NR^{14}R^{15}$ (R^{14} and R^{15} are each independently hydrogen, C_1-C_6 alkyl or aryl,

formulas (VI), (VII) and (VIII)



(VI) (VII) (VIII)

wherein R^{16} and R^{17} are each independently hydrogen, C_1 -C_6 alkyl, alkoxy, halogen, cyano, nitro, amino, trifluoromethyl or carboxyl, R^{18} and R^{19} are each independently hydrogen or C_1 -C_6 alkyl, and Y' is oxygen or sulfur.

13. (New) A pharmaceutical composition for the diseases caused by an excessive effect of NAD(P)H oxidase, which comprises the agent of claim 6 as an active ingredient.

14. (New) The pharmaceutical composition of claim 13, which is administered simultaneously with a hypolipidemic agent, an antihypertensive agent, a hypoglycemic agent, a vasodilator, an antiplatelet agent, an anticoagulant, a brain protective agent, an anticancer agent, a diuretic agent, a cardiotonic agent, an analgesic agent, an antiedemic agent, a thrombolytic agent, an immunosuppressant, a steroid, a vitamin or an antioxidant, or administered separately therefrom, or administered sequentially therewith.